Press, New York, 1991). In a preferred embodiment, the percent identity between two amino acid sequences is determined using the Needleman and Wunsch (J. Mol. Biol. (48):444-453 (1970)) algorithm which has been incorporated into the GAP program in the GCG software package, using either a Blossom 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. In yet another preferred embodiment, the percent identity between two nucleotide sequences is determined using the GAP program in the GCG software package (Devereux, J., et al., Nucleic Acids Res. 12(1):387 (1984)), using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. In another embodiment, the percent identity between two amino acid or nucleotide sequences is determined using the algorithm of E. Meyers and W. Miller (CABIOS, 4:11-17 (1989)) which has been incorporated into the ALIGN program (version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4.

C1

Please replace the first paragraph on page 13 with the following paragraph ("paragraph 2"):

The nucleic acid and protein sequences of the present invention can further be used as a "query sequence" to perform a search against sequence databases to, for example, identify other family members or related sequences. Such searches can be performed using the NBLAST and XBLAST programs (version 2.0) of Altschul, et al. (J. Mol. Biol. 215:403-10 (1990)). BLAST nucleotide searches can be performed with the NBLAST program, score = 100, word length = 12 to obtain nucleotide sequences homologous to the nucleic acid molecules of the invention. BLAST protein searches can be performed with the XBLAST program, score = 50, word length = 3, to obtain amino acid sequences homologous to the proteins of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul et al. (Nucleic Acids Res. 25(17):3389-3402 (1997)). When utilizing BLAST and gapped BLAST programs, the default parameters of the respective programs (e.g., XBLAST and NBLAST) can be used.

C2

Please replace the last paragraph on page 3 (which wraps around to the top of page 4) with the following paragraph ("Paragraph 3"):

Despite their sequence variations, all five subfamilies of the Ras superfamily share conserved structural features. Four conserved sequence regions (motifs I-IV) have been studied in

C3

the LMW GTP-binding proteins. Motif I is the most variable but has the conserved sequence, GXXXXGK (SEQ ID NO:6). The lysine residue is essential in interacting with the .beta.- and .gamma.-phosphates of GTP. Motif II, III, and IV contain highly conserved sequences of DTAGQ (SEQ ID NO:7), NKXD (SEQ ID NO:8), and EXSAX (SEQ ID NO:9), respectively. Specifically, Motif II regulates the binding of gamma-phosphate of GTP; Motif III regulates the binding of GTP; and Motif IV regulates the guanine base of GTP. Most of the membrane-bound LMW GTP-binding proteins generally require a carboxy terminal isoprenyl group for membrane association and biological activity. The isoprenyl group is added posttranslationally through recognition of a terminal cysteine residue alone or a terminal cysteine-aliphatic amino acid-aliphatic amino acid-any amino acid (CAAX; SEQ ID NO:10) motif. Additional membrane-binding energy is often provided by either internal palmitoylation or a carboxy terminal cluster of basic amino acids. The LMW GTP-binding proteins also have a variable effector region, located between motifs I and II, which is characterized as the interaction site for guanine nucleotide exchange factors (GEFs) or GTPase-activating proteins (GAPs). GEFs induce the release of GDP from the active form of the G protein, whereas GAPs interact with the inactive form by stimulating the GTPase activity of the G protein.

C3

Please replace the last full paragraph on page 4 with the following paragraph ("Paragraph 4"):

A number of Rho GTP-binding proteins have been identified in plasma membrane and cytoplasm. These include RhoA, B and C, and D, rhoG, rac 1 and 2, G25K-A and B, and TC10 (Hall, A. et al. (1993) Philos. Trans. R. Soc. Lond. (Biol.) 340:267-271). All Rho proteins have a CAAX (SEQ ID NO:10) motif which binds a prenyl group and either a palmitoylation site or a basic amino acid-rich region, suggesting their role in membrane-associated functions. In particular, RhoD is a protein which functions in early endosome motility and distribution by inducing rearrangement of actin cytoskeleton and cell surface (Murphy, C. et al. (1996) Nature 384:427-432). During cell adhesion, the Rho proteins are essential for triggering focal complex assembly and integrin-dependent signal transduction (Hotchin, N. A. and Hall, A. (1995) J. Cell Biol. 131:1857-1865).

C4

Please replace the last paragraph on page 4 (which wraps around to the top of page 5) with the following paragraph ("Paragraph 5"):

The Ras subfamily proteins already indicated supra are essential in transducing signals from receptor tyrosine kinases (RTKs) to a series of serine/threonine kinases which control cell growth and differentiation. Mutant Ras proteins, which bind but cannot hydrolyze GTP, are permanently activated and cause continuous cell proliferation or cancer. TC21, a Ras-like protein, C5 is found to be highly expressed in a human teratocarcinoma cell line (Drivas, G. T. et al. (1990) Mol. Cell. Biol. 10: 1793-1798). Rin and Rit are characterized as membrane-binding, Ras-like proteins without the lipid-binding CAAX (SEQ ID NO:10) motif and carboxy terminal cysteine (Lee, C.-H. J. et al. (1996) J. Neurosci. 16: 6784-6794). Further, Rin is shown to localize in neurons and have calcium-dependant calmodulin-binding activity.

**Version of Amended Specification Paragraphs With Markings to Show Changes Made:**

*NOTE: Deletions are marked by brackets and bold text; insertions are marked by underlining and bold text.*

Paragraph 1:

The comparison of sequences and determination of percent identity and similarity between two sequences can be accomplished using a mathematical algorithm. (Computational Molecular Biology, Lesk, A.M., ed., Oxford University Press, New York, 1988; Biocomputing: Informatics and Genome Projects, Smith, D.W., ed., Academic Press, New York, 1993; Computer Analysis of Sequence Data, Part 1, Griffin, A.M., and Griffin, H.G., eds., Humana Press, New Jersey, 1994; Sequence Analysis in Molecular Biology, von Heinje, G., Academic Press, 1987; and Sequence Analysis Primer, Gribskov, M. and Devereux, J., eds., M Stockton Press, New York, 1991). In a preferred embodiment, the percent identity between two amino acid sequences is determined using the Needleman and Wunsch (J. Mol. Biol. (48):444-453 (1970)) algorithm which has been incorporated into the GAP program in the GCG software package **[(available at http://www.gcg.com)]**, using either a Blossom 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. In yet another preferred embodiment, the percent identity between two nucleotide sequences is determined using the GAP program in the GCG software package (Devereux, J., et al., Nucleic Acids Res. 12(1):387 (1984)) **[(available at http://www.gcg.com)]**, using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. In another embodiment, the percent identity between two amino acid or nucleotide sequences is determined using the algorithm of E. Meyers and W. Miller (CABIOS, 4:11-17 (1989)) which has been incorporated into the ALIGN program (version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4.

Paragraph 2:

The nucleic acid and protein sequences of the present invention can further be used as a "query sequence" to perform a search against sequence databases to, for example, identify other family members or related sequences. Such searches can be performed using the NBLAST and

XBLAST programs (version 2.0) of Altschul, et al. (J. Mol. Biol. 215:403-10 (1990)). BLAST nucleotide searches can be performed with the NBLAST program, score = 100, word length = 12 to obtain nucleotide sequences homologous to the nucleic acid molecules of the invention. BLAST protein searches can be performed with the XBLAST program, score = 50, word length = 3, to obtain amino acid sequences homologous to the proteins of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul et al. (Nucleic Acids Res. 25(17):3389-3402 (1997)). When utilizing BLAST and gapped BLAST programs, the default parameters of the respective programs (e.g., XBLAST and NBLAST) can be used. **[See http://www.ncbi.nlm.nih.gov.]**

Paragraph 3:

Despite their sequence variations, all five subfamilies of the Ras superfamily share conserved structural features. Four conserved sequence regions (motifs I-IV) have been studied in the LMW GTP-binding proteins. Motif I is the most variable but has the conserved sequence, GXXXXGK **(SEQ ID NO:6)**. The lysine residue is essential in interacting with the .beta.- and .gamma.-phosphates of GTP. Motif II, III, and IV contain highly conserved sequences of DTAGQ **(SEQ ID NO:7)**, NKXD **(SEQ ID NO:8)**, and EXSAX **(SEQ ID NO:9)**, respectively. Specifically, Motif II regulates the binding of gamma-phosphate of GTP; Motif III regulates the binding of GTP; and Motif IV regulates the guanine base of GTP. Most of the membrane-bound LMW GTP-binding proteins generally require a carboxy terminal isoprenyl group for membrane association and biological activity. The isoprenyl group is added posttranslationally through recognition of a terminal cysteine residue alone or a terminal cysteine-aliphatic amino acid-aliphatic amino acid-any amino acid (CAAX**; SEQ ID NO:10**) motif. Additional membrane-binding energy is often provided by either internal palmitoylation or a carboxy terminal cluster of basic amino acids. The LMW GTP-binding proteins also have a variable effector region, located between motifs I and II, which is characterized as the interaction site for guanine nucleotide exchange factors (GEFs) or GTPase-activating proteins (GAPs). GEFs induce the release of GDP from the active form of the G protein, whereas GAPs interact with the inactive form by stimulating the GTPase activity of the G protein.

Paragraph 4:

A number of Rho GTP-binding proteins have been identified in plasma membrane and cytoplasm. These include RhoA, B and C, and D, rhoG, rac 1 and 2, G25K-A and B, and TC10 (Hall, A. et al. (1993) Philos. Trans. R. Soc. Lond. (Biol.) 340:267-271). All Rho proteins have a CAAX **(SEQ ID NO:10)** motif which binds a prenyl group and either a palmitoylation site or a basic amino acid-rich region, suggesting their role in membrane-associated functions. In particular, RhoD is a protein which functions in early endosome motility and distribution by inducing rearrangement of actin cytoskeleton and cell surface (Murphy, C. et al. (1996) Nature 384:427-432). During cell adhesion, the Rho proteins are essential for triggering focal complex assembly and integrin-dependent signal transduction (Hotchin, N. A. and Hall, A. (1995) J. Cell Biol. 131:1857-1865).

Paragraph 5:

The Ras subfamily proteins already indicated supra are essential in transducing signals from receptor tyrosine kinases (RTKs) to a series of serine/threonine kinases which control cell growth and differentiation. Mutant Ras proteins, which bind but cannot hydrolyze GTP, are permanently activated and cause continuous cell proliferation or cancer. TC21, a Ras-like protein, is found to be highly expressed in a human teratocarcinoma cell line (Drivas, G. T. et al. (1990) Mol. Cell. Biol. 10: 1793-1798). Rin and Rit are characterized as membrane-binding, Ras-like proteins without the lipid-binding CAAX **(SEQ ID NO:10)** motif and carboxy terminal cysteine (Lee, C.-H. J. et al. (1996) J. Neurosci. 16: 6784-6794). Further, Rin is shown to localize in neurons and have calcium-dependant calmodulin-binding activity.